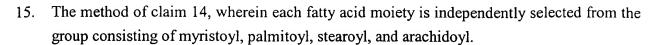
15

We claim:

A method for modulating the immune function of an animal comprising administering to the animal a therapeutic amount of a hedgehog or ptc therapeutic.

10

- A method for suppressing the immune system of an animal comprising contacting the cells with an effective amount of a hedgehog protein, or agonist thereof.
- 3. A method for enhancing the immune system of an animal comprising administering to a immunostimulatory amount of/a hedgehog antagonist.
- The method of any of claims 1, wherein the hedgehog therapeutic is a polypeptide which 4. includes a hedgehog amino acid sequence which is identical or homologous to an amino acid sequence of any one of SEQ ID Nos. 10-18.
- 5. The method of claim 4, wherein the hedgehog amino acid sequence is sufficient for specific binding of the polypeptide to a patched protein.
- 6. The method of claim 4, wherein the hedgehog amino acid sequence is at least 80 percent identical to an amino acid sequence of any one of SEQ ID Nos. 10-18.
- 7. The method of claim 4, wherein the hedgehog amino acid sequence is encodable by a nucleic acid which hybridizes under stringent conditions to any one of SEQ ID Nos. 1-9.
- 8. The method of claim 4, wherein the hedgehog amino acid sequence is of a vertebrate hedgehog protein.
- 9. The method of claim 4, wherein the polypeptide includes at least a 50 amino acid extracellular portion of a vertebrate hedgehog protein.
- The method of claim 4, wherein the polypeptide includes at least an extracellular portion of a vertebrate hedgehog protein corresponding to residues 24-194 of SEQ ID No:15.
- The method of claim 4, wherein the hedgehog polypeptide is modified with one or more 25 lipophilic moieties.
 - The method of claim 11, wherein the hedgehog polypeptide is modified with one or more sterol moieties.
 - The method of claim 12, wherein the sterol moiety is cholesterol.
- The method of claim 11, wherein the hedgehog polypeptide is modified with one or more 30 fatty acid moieties.



- 16. The method of claim 11, wherein the hedgehog polypeptide is modified with one or more aromatic hydrocarbons.
- 17. The method of claim 16, wherein each aromatic hydrocarbon is ondependently selected from the group consisting of benzene, perylene, phenanthrene, anthracene, naphthalene, pyrene, chrysene, and naphthacene.
- 18. The method of claim 11, wherein the hedgehog polypeptide is modified one or more times with a C7 C30 alkyl or cycloalkyl.
- 10 19. The method of claim 1, wherein the ptc therapeutic is a small organic molecule.
 - 20. The method of claim 19, wherein the binding of the ptc therapeutic to *patched* results in upor down-regulation of patched and/or gli expression.
 - 21. The method of claim 1, wherein the *ptc* therapeutic binds to *patched* and mimics *hedgehog*-mediated *patched* signal transduction.
 - 22. The method of claim 19, wherein the ptc therapeutic is an inhibitor of protein kinase A.
 - 23. The method of claim 22, wherein the PKA inhibitor is a 5-isoquinolinesulfonamide
 - 24. The method of claim 22, wherein the PKA inhibitor is represented in the general formula:

wherein,

R₁ and R₂ each can independently represent hydrogen, and as valence and stability permit a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, -(CH₂)_m-R₈, -(CH₂)_m-OH, -(CH₂)_m-O-lower alkyl, -(CH₂)_m-O-lower alkenyl, -(CH₂)_n-O-lower

5

10

 $(CH_2)_m$ -R₈, - $(CH_2)_m$ -SH, - $(CH_2)_m$ -S-lower alkyl, - $(CH_2)_m$ -S-lower alkenyl, - $(CH_2)_m$ -S- $(CH_2)_m$ -R₈, or

R₁ and R₂ taken together with N form a heterocycle (substituted or unsubstituted);

 R_3 is absent or represents one or more substitutions to the isoquinoline ring such as a lower alkyl, a lower alkenyl, a lower alkynyl, a carbonyl (such as a carboxyl, an ester, a formate, or a ketone), a thiocarbonyl (such as a thioester, a thioacetate, or a thioformate), an amino, an acylamino, an amido, a cyano, a nitro, an azido, a sulfate, a sulfonate, a sulfonamido, $-(CH_2)_m$ - R_8 , $-(CH_2)_m$ -O-lower alkyl, $-(CH_2)_m$ -O-lower alkenyl, $-(CH_2)_m$ -O-($-(CH_2)_m$ - $-(CH_2)_m$ -S-lower alkyl, $-(CH_2)_m$ -S-lower alkenyl, $-(CH_2)_m$ -S-($-(CH_2)_m$ - $-(CH_2)_m$ -S-lower alkyl, $-(CH_2)_m$ -S-lower alkenyl, $-(CH_2)_m$ -S-($-(CH_2)_m$ -S-($-(CH_2)_m$ -S-lower alkyl, $-(CH_2)_m$ -S-lower alkenyl, $-(CH_2)_m$ -S-($-(CH_2)_m$ -S-($-(CH_2)_m$ -S-lower alkyl, $-(CH_2)_m$ -S-($-(CH_2)_m$ -S-($-(CH_2)_m$ -S-($-(CH_2)_m$ -S-lower alkyl, $-(CH_2)_m$ -S-($-(CH_2)_m$ -

 R_8 represents a substituted or unsubstituted aryl, aralkyl, cycloalkyl, cycloalkenyl, or heterocycle; and

n and m are independently for each occurrence zero or an integer in the range of 1 to 6.

- 25. The method of claim 22, wherein the PKA inhibitor is cyclic AMP analog.
- 26. The method of claim 22, wherein the PKA inhibitor is selected from the group consisting of N-[2-((p-bromocinnamyl)amino)ethyl]-5-isoquinolinesulfonamide, 1-(5-isoquinolinesulfonyl)-2-methylpiperazine, KT5720, 8-bromo-cAMP, dibutyryl-cAMP and PKA Heat Stable Inhibitor isoform α.
- 27. A therapeutic preparation of a small molecule antagonist of *patched*, which *patched* antagonist is provided in a pharmaceutically acceptable carrier and in an amount sufficient to modulate the immune system of an adult human patient.
- 2\(\beta \). A method for modulating T lymphocytes maturation, comprising administering to a patient a gene activation construct which recombines with a genomic *hedgehog* gene of the patient to provide a heterologous transcriptional regulatory sequence operatively linked to a coding sequence of the *hedgehog* gene.
- 25 29. A method of claim 2, wherein suppressing the immune function of an animal comprises inhibiting T lymphocyte maturation.
 - 30. A method of claim 3, wherein enhancing the immune function of an animal comprises stimulating T lymphocyte maturation.

